

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD.,)	
)	
Plaintiff,)	
)	
v.)	C.A. No. 21-1015 (GBW)
)	
SAREPTA THERAPEUTICS, INC.,)	VOLUME 1 (Part 1) (Exhibits 1-4)
)	
Defendant.)	

SAREPTA THERAPEUTICS, INC.,)	
)	
Defendant and Counter-Plaintiff,)	
)	
v.)	
)	
NIPPON SHINYAKU CO., LTD.)	
and NS PHARMA, INC.)	
)	
Plaintiff and Counter-)	
Defendants.)	

**JOINT APPENDIX TO CLAIM CONSTRUCTION BRIEF
FOR THE WILTON/UWA PATENTS**

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JOINT APPENDIX

Exhibit Number	Description
1	U.S. Patent No. 9,994,851
2	U.S. Patent No. 10,227,590
3	U.S. Patent No. 10,266,827
4	Aartsma-Rus et al., “Targeted Exon Skipping as a Potential Gene Correction Therapy for Duchenne Muscular Dystrophy,” <i>Neuromuscul. Disord.</i> (2002) 12: S71-S77 (“Aartsma-Rus 2002”)
5	Aartsma-Rus et al., “Antisense-Mediated Exon Slipping: A Versatile Tool with Therapeutic and Research Applications,” <i>RNA</i> (2007) 13(10): 1609-1624 (“Aartsma-Rus 2007”)
6	Arora et al., “Neutrally Charged Phosphorodiamidate Morpholino Antisense Oligomers: Uptake, Efficacy and Pharmacokinetics,” <i>Curr. Pharm. Biotechnol.</i> (2004) 5(5): 431-439 (“Arora 2004”)
7	Alberts et al., <i>Molecular Biology of the Cell</i> 191-234, 299-374 (4th ed. 2002) (“Alberts 2002”)
8	Botvin Madorsky at al., “Psychosocial Aspects of Death and Dying in Duchenne Muscular Dystrophy,” <i>Arch. Phys. Med. Rehabil.</i> (1984) 65(2): 79-82 (“Botvin Madorsky 1984”)
9	Exondys 51 [®] (Eteplirsen) Prescribing Information (Revised: 1/2022) (“Eteplirsen Label”)
10	European Patent No. 2206781 B1
11	Nippon Shinyaku Co. Ltd., Opposition Against European Patent No. 2206781 B1 (“NS Notice of Opposition”)
12	FDA News Release dated September 19, 2016 (“FDA 2016”)
13	FDA News Release dated December 12, 2019 (“FDA 2019”)
14	FDA News Release dated August 12, 2020 (“FDA 2020”)
15	Vyondys 53 [®] (Golodirsen) Prescribing Information (Revised: 2/2021) (“Golodirsen Label”)
16	Hoffman et al., “Conservation of the Duchenne Muscular Dystrophy Gene in Mice and Humans,” <i>Science</i> (1987) 238(4825): 347-350 (“Hoffman 1987”)
17	Interference No. 106,007, Decision dated May 12, 2016
18	Koenig et al., “The Complete Sequence of Dystrophin Predicts a Rod-Shaped Cytoskeletal Protein,” <i>Cell</i> (1988) 53(2):219-228 (“Koenig 1988”)
19	Mann et al., “Improved Antisense Oligonucleotide Induced Exon Skipping in the Mdx Mouse Model of Muscular Dystrophy,” <i>J. Gene Med.</i> (2002) 4(6): 644-654
20	Prosecution History Excerpt of U.S. Application No. 15/273,772
21	Prosecution History Excerpt of U.S. Patent No. 9,708,361
22	Prosecution History Excerpt of U.S. Patent No. 9,994,851
23	Prosecution History Excerpt of U.S. Patent No. 10,266,827
24	Summerton et al., “Morpholino Antisense Oligomers: Design, Preparation, and Properties,” <i>Antisense Nucleic Acid Drug Dev.</i> (1997) 7(3): 187-195 (“Summerton 1997(a)”)

Exhibit Number	Description
25	Summerton et al., “Morpholino and Phosphorothioate Antisense Oligomers Compared in Cell-Free and In-Cell Systems,” <i>Antisense Nucleic Acid Drug Dev.</i> (1997) 7(2): 63-70 (“Summerton 1997(b)”)
26	Summerton, “Morpholino Antisense Oligomers: The Case for an RNase H-Independent Structural Type,” <i>Biochim. Biophys. Acta</i> (1999) 1489(1): 141-158 (“Summerton 1999”)
27	Summerton, “Mopholinos and PNAs Compared,” <i>Lett. Pept. Sci.</i> (2003) 10: 215-236 (“Summerton 2003”)
28	Suzuki et al., “Gene Therapy for Duchenne Muscular Dystrophy,” <i>Future Neurol.</i> (2006) 2(1): 87-96 (“Suzuki 2007”)
29	U.S. Patent No. 9,708,361
30	van Deutekom et al., “Antisense-Induced Exon Skipping Restores Dystrophin Expression in DMD Patient Derived Muscle Cells,” <i>Hum. Mol. Genet.</i> (2001) 10(15): 1547-1554 (“van Deutekom 2001”)
31	Viltepso® (Viltolarsen) Prescribing Information (Revised: 3/2021) (“Viltolarsen Label”)
32	Wilton et al., “Specific Removal of the Nonsense Mutation from the Mdx Dystrophin mRNA Using Antisense Oligonucleotides,” <i>Neuromuscul. Disord.</i> (1999) 9(5):330-338 (“Wilton 1999”)
33	Wilton et al., “Antisense Oligonucleotides, Exon Skipping and the Dystrophin Gene Transcript,” <i>Acta Myol.</i> (2005) 24(3): 222-229 (“Wilton 2005”)
34	Aartsma-Rus et al., “Less is More: Therapeutic Exon Skipping for Duchenne Muscular Dystrophy,” <i>Lancet Neurol.</i> (2009) 8(10): 873-875 (“Aartsma-Rus 2009”)
35	Swanson, “FDA Approves Sarepta Therapeutics’ Vyondys 53 for Treatment of DMD Amenable to Exon 53 Skipping,” Muscular Dystrophy Association: Quest (December 13, 2019), https://mdaquest.org/fda-approves-sarepta-therapeutics-vyondys-53-for-treatment-of-dmd-amenable-to-exon-53-skipping/ (“MDA 2019”)
36	Excerpt of Nippon Shinyaku Co. Ltd.’s Initial Invalidity Contentions, <i>Nippon Shinyaku Co., Ltd., v. Sarepta Therapeutics, Inc.</i> , No. 21-1015 (MN) (D. Del. Jul. 18, 2022)
37	Opening Declaration of Cy A. Stein, M.D., Ph.D. dated January 4, 2023
38	U.S. Patent No. 8,084,601
39	Gene Tools, LLC, <i>Morpholino History, Production, and Properties</i> , available at https://www.gene-tools.com/history_production_and_properties (last accessed Feb. 6, 2023)
40	Helm, J., <i>Towards Personalized Allele-Specific Antisense Oligonucleotide Therapies for Toxic Gain-of Function Neurodegenerative Diseases</i> , Pharmaceutics 2022, 14, 1708
41	LEQVIO Prescribing Information, Revised 12/2021
42	The Writing Center, Parallel Structure available at https://writingcenter.gmu.edu/writing-resources/grammar-style/parallel-structure (last accessed Feb. 6, 2023)
43	Declaration of Michelle L. Hastings, Ph.D.

Exhibit Number	Description
44	Merriam Webster Online Dictionary definition of “within” available at https://www.merriam-webster.com/dictionary/within (last accessed Feb. 6, 2023)
45	Prosecution History Excerpt of RE47,691
46	Grammar Monster definition of “non-restrictive clause” available at https://www.grammar-monster.com/glossary/non-restrictive_clauses.htm (last accessed Feb. 6, 2023)
47	Koenig et al., “Complete Cloning of the Duchenne Muscular Dystrophy (DMD) cDNA and Preliminary Genomic Organization of the DMD Gene in Normal and Affected Individuals,” <i>Cell</i> (1987) 50(3):509-517 (“Koenig 1987”)
48	Havens et al., “Targeting RNA Splicing for Disease Therapy,” <i>WIREs RNA</i> (2013) 4(3): 247-266 (“Havens 2013”)
49	Havens et al., “Splice-Switching Antisense Oligonucleotides as Therapeutic Drugs,” <i>Nucleic Acids Res.</i> (2016) 44(14): 6549-6563 (“Havens 2016”)
50	Takeda et al., “Exon-Skipping in Duchenne Muscular Dystrophy,” <i>J. Neuromuscul. Dis.</i> (2021) 8(s2): S343-S358 (“Takeda 2021”)
51	Merriam-Webster, Inc., <i>Merriam-Webster’s Collegiate Dictionary</i> 1341 (10th ed. 2000) (“Merriam-Webster Dictionary”)
52	Univ. of Chi. Press, <i>The Chicago Manual of Style Online</i> § 6.19, https://www.chicagomanualofstyle.org/book/ed17/part2/ch06/psec019.html (last visited Feb. 21, 2023)
53	Reply Declaration of Cy A. Stein, M.D., Ph.D. dated February 27, 2023